In The United States Patent Office

In re Albert M. FLEISCHNER, Ph.D., "Herbal Composition for Weight Control"	Technology Center 1655 Serial No. 10/693,442 Filed 23 October 2003
	APPEAL BRIEF

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I. INTRODUCTION

This APPEAL BRIEF is submitted pursuant to the earlier-submitted NOTICE OF APPEAL. Enclosed please find the large-entity fee for filing an appeal brief. This APPEAL BRIEF is filed within two months of the earlier-submitted NOTICE OF APPEAL. No extension of time fee is therefore believed due.

This patent application has been granted Special status. Expedited resolution of this appeal is therefore respectfully requested.

A. Real Party In Interest

The real party in interest is TrimSpa Corporation, a New Jersey corporation.

B. Related Appeals and Interferences

There are no related appeals nor interferences known to appellant, the appellant's legal representative, nor the assignee which may be related to, directly affect nor be directly affected by or have a bearing on the Board's decision in the immediate appeal.

C. Status of Claims

Claims 8 to 16 and 27 stand canceled. Claims 1 to 7, 17 to 26 and 28 to 40 stand twice rejected. Appellant appeals the rejection of all pending claims.

D. Status of Amendments

No amendment has been filed subsequent to a final rejection.

E. Summary of Claimed Subject Matter

Hoodia gordonii is a cactus. *See* SPECIFICATION at page 3, line 3. The prior art teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one, a compound naturally present in *Hoodia gordonii*, temporarily suppresses hunger, then stimulates hunger, causing a net increase in body weight. *Id.* at page 3, line 8 to page 4, line 21. That compound thus appears suitable for investigation as, *e.g.*, a body-building supplement. In contrast, the Inventor has found that *Hoodia gordonii* can be used to reduce excess body weight and maintain a healthy lower body weight.

Independent claim number 1 is drawn to a method of body weight reduction comprising administering a body weight reducing amount of *hoodia gordonii* at least once every 48 hours, for about 45 days. *Id.* at page 5, line 10 *et seq*.

Dependent claim number 2 is drawn to a method of body weight reduction comprising administering *hoodia gordonii* at least three times every 24 hours, for about 45 days. *Id.* at page 6, line 3 *et seq*.

Dependent claim number 3 is drawn to a method of body weight reduction comprising administering *hoodia gordonii* and a second compound

selected from the group consisting of a stimulant and glucosamine, for about 45 days. *Id.* at page 6, line 7 *et seq.*

Independent claim 19 is drawn to a composition of matter for body weight reduction, comprising *hoodia gordonii* and a second compound (a stimulant and/or glucosamine). *Id.*

Independent claim 35 is drawn to a method of body weight reduction comprising administering *hoodia gordonii* in an amount sufficient to suppress the appetite, said administration repeated a plurality of times, each one of said times occurring before the *hoodia gordonii* causes an appetite stimulating effect. *Id.* at page 5, line 22 *et seq.*

F. Grounds of Rejection to be Reviewed on Appeal

The grounds for rejection presented on appeal are as follows:

i. Whether the OFFICE ACTION states a *prima facie* case of failure to comply with the "written description" requirement of Section 112, first paragraph?

ii. Whether the OFFICE ACTION states a *prima facie* case of failure to comply with the enablement requirement of Section 112, first paragraph?

iii. Whether the OFFICE ACTION states a *prima facie* case of obviousness under Section 103?

G. Argument

Applicant respectfully believes the application presents four groups of claims, each group independently patentable *viz* the art of record:

Claim 1 - *Hoodia gordonii* for weight control

Claim 2 – *Hoodia gordonii* Intensive administration regimen

Claims 3, 19 and 37 – *Hoodia gordonii* combined with glucosamine or a stimulant.

Claim 35 – An administration regimen for *Hoodia gordonii.*

The claim groups argued separately from claim 1 are placed under sub-headings including the relevant claim number.

II. THE OFFICE ACTION FAILS TO STATE A *PRIMA FACIE* CASE OF NON-COMPLIANCE WITH 35 U.S.C. § 112, FIRST PARAGRAPH

A. The Original Disclosure Provides Adequate Written Description For Dependent Claims 23-26 And 28-34

The OFFICE ACTION alleges that the original disclosure fails to provide an adequate written description supporting dependent claims 23-26 and 28-34. The OFFICE ACTION, however, fails to state a *prima facie* case.

1. The Examiner Must Provide Evidence Showing That The Disclosure Fails To Support The Claimed Invention

To satisfy the written description requirement, the original disclosure must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir., 2003). The original disclosure includes both the specification and the claims originally filed. *E.g., In re Benno*, 768 F.2d 1340 (Fed. Cir. 1985); *In re Koller*, 613 F.2d 819 (C.C.P.A., 1980). Thus, most of the "written description" caselaw addresses whether the disclosure as originally filed provides adequate support for amendments to the claims or the specification. *See e.g., In re Lukach*, 442 F.2d 967 (C.C.P.A., 1971); *Martin v. Mayer*, 823 F.2d 500, 503 (Fed. Cir. 1987).

In contrast, there is a strong presumption that an adequate "written description of the claimed invention is present in the disclosure as filed. *See In re Wertheim*, 541 F.2d 257, 263 (C.C.P.A., 1976). Thus, the Patent Office bears the burden of presenting evidence showing that the original disclosure fails to show possession of the claimed invention. *Id.*

2. The Examiner Fails To Provide Evidence That The Disclosure Does Not Support Claims 23-26 And 28-34

In the immediate case, independent claim 19 covers " A composition of matter for body weight reduction, comprising a body weight reducing amount of *hoodia gordonii* together with a second compound selected from the group consisting of a stimulant and glucosamine." In contrast, claims 23-26 and 28-34 depend from claim 19, and specify particular amounts of stimulant or glucosamine.

The Examiner acknowledges that claim 19 is part of the original disclosure, and therefore is adequately supported by it. The Examiner, however, argues that dependent claims 23-26 and 28-34 impermissibly "broaden" the concept of independent claim 19:

> [claims 23-26 and 28-34] broaden the concept of the originally disclosed / claimed invention – i.e., the original disclosure and claims were limited to disclosed effective amounts (e.g., particular ranges) of one or more of the ingredients recited. ... the original specification including the original claims do not support the concept of any and all undefined amount(s) of the recited ingredients.

Applicant respectfully disagrees, for two reasons.

First, dependent claims cannot "broaden" an independent claim as a matter of law.

Second, the "concept of the originally disclosed claimed invention" was not "limited to disclosed effective amounts (e.g., particular ranges)" of

stimulant and/or glucosamine. To the contrary, claim 19 uses the transitional phrase "comprising." In so doing, claim 19 provides a written description of a composition including *hoodia gordonii* and a stimulant and/or glucosamine, alone or together with any other ingredient(s), regardless of how much stimulant, regardless of how much glucosamine, and regardless of how much other ingredient(s) is present.[1]

The disputed claims depend from claim 19, and merely add to the basic invention of claim 19 additional limitations. As dependent claims, the disputed claims cannot "broaden the concept of" the invention of claim 19.

B. The OFFICE ACTION Fails To State A *Prima Facie* Case Of Non-Enablement For Claims 1-7, 17-26 and 28-40

The OFFICE ACTION argues that claims 1-7, 17-26 and 28-40 are not deemed enabled without "evidence [] that the claimed biological material (*e.g.*, the required amount of seeds from the instantly claimed plant *Hoodia gordonii*) is

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[1] The transitional phrase "consisting of" excludes any ingredient not specified in the claim. *E.g., Ex parte Gray*, 53 F.2d 520 (C.C.P.A. 1931). In contrast, the transitional phrase "comprising" is open-ended, and allows for additional ingredients not expressly recited in the claim. *E.g., Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir., 1997); *Moleculon Res. Corp. v. CBS, Inc.*, 793 F.2d 1261 (Fed. Cir. 1986); *In re Baxter*, 656 F.2d 679, 686 (C.C.P.A., 1981); *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I., 1948) (the transitional phrase "comprising" leaves "the claim open for the inclusion of ingredients even in major amounts").

known and readily available." The OFFICE ACTION thus alleges that the correct legal test is that Hoodia gordonii be both known and readily available.

The OFFICE ACTION fails to state a *prima facie* case of non-enablement for several reasons.

First, the OFFICE ACTION fails to address the claimed invention. The OFFICE ACTION demands evidence that "the claimed biological material" is known and available. The claims are not, however, drawn to "biological material." Rather, the claims are drawn to methods for using a plant, and compositions including that plant.

Second, the administrative agency record shows that *Hoodia gordonii* is "known." Evidence showing that *Hoodia gordonii* is known includes, for example, the prior art which the Examiner relies on to argue that the claimed invention is obvious. Put another way, the Examiner's allegation that *Hoodia gordonii* is known in the art for purposes of Section 103, contradicts his allegation that it is unknown for purposes of Section 112, first paragraph.

Third, the agency record shows that *Hoodia gordonii* is readily available. Applicant's PETITION TO MAKE EXAMINATION SPECIAL made of record evidence showing that Applicant's TrimSpa® brand *Hoodia gordonii* product is

readily available, as are various competitors' slavish copies of it.[2] Indeed, since the filing of the immediate application, Applicant's TrimSpa® product has enjoyed a singular commercial success; this success has in turn induced widespread copying. *See* INFORMATION DISCLOSURE STATEMENT (7 May 2006) (making of record evidence showing that copies of the Applicant's *Hoodia gordonii* product is now available from, *inter alia,* hoodoba.com, weightlossguide.com, h57.com, hoodithin.com and phenterlean.com.) The factual record before the agency therefore shows that *Hoodia gordonii* is readily available.

The OFFICE ACTION (10 Feb. 2006) argues that "this cactus plant only grows wild in the Kalahari Desert." Assuming that this factual allegation is true,[3] where something "grows wild" is not the applicable legal standard. Rather, the applicable legal standard is whether the disclosure as a whole, read in the context of the knowledge of the art, enables one of skill in the art to practice the claimed invention.

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[2] If imitation be the sincerest form of flattery, these products show it abundantly; the TrimSmart™, TrimClub™ and HoodiaSpa™ products not only copy Applicant's product, but also Applicant's packaging, label graphics and trademarks!

[3] It might not be. The record shows that *Hoodia gordonii* grows wild in the Kalahari Desert. The record, however, fails to show that *Hoodia gordonii* **only** grows in the Kalahari Desert.

In the immediate case, the Examiner does not dispute that one of skill in the art can practice the claimed invention. To the contrary, the agency record shows that since the immediate patent application was published (in December of 2004), numerous parties *are in fact actually practicing the claimed invention* in The United States. *See e.g.*, PETITION TO MAKE EXAMINATION SPECIAL UNDER 37 C.F.R. § 1.17(H) (9 July 2005); INFORMATION DISCLOSURE STATEMENT (7 May 2006); Martina HABECK, *A Succulent Cure To End Obesity*, 7 DRUG DISCOV. TODAY 280 (March 2002) at Figure 1 (photograph of *Hoodia* seedlings being propagated in a greenhouse in Godmanchester, United Kingdom); Albert M. Fleischner, DECLARATION (13 June 2006) at ¶¶ 8-9; Ian B. OLIVER, *Grow Succulents* (2003) (teaching that *Hoodia* cactus may be cultivated outside of the Kalahari desert, that it makes a wonderful container plant and that it looks handsome in terra cotta containers).

The administrative agency record therefore shows that *Hoodia gordonii* is known in the art, and is available both commercially and as a cultivar.

III. THE OFFICE ACTION FAILS TO STATE A *PRIMA FACIE* CASE OF OBVIOUSNESS

A *prima facie* case of obviousness requires three elements. *In re Vaeck*, 947 F.2d 488 (Fed.Cir. 1991). First, the prior art must teach each element of the claims at issue. Second, the prior art must teach a reasonable expectation of

success. Third, the prior art must suggest modifying the prior art to replicate the claimed invention. In the instant case, the prior art fails to fulfill any of these three elements.

A. The References Relied on By the Examiner

The OFFICE ACTION relies on the following prior art references to show obviousness:

I. Fanie Retief VAN HEERDEN *et al.*, *Pharmaceutical Compositions Having Appetite Suppressant Activity*, U.S. Letters Patent No. 6,376,657, teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one, a compound which occurs naturally in *Hoodia gordonii,* causes transient appetite suppression followed by appetite stimulation and a net body weight gain.

II. Martina HABECK, *A Succulent Cure To End Obesity*, 7 DRUG DISCOV. TODAY 280 (March, 2002) teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one does not cause weight loss.

III. Anthony BARNETT, *In Africa the Hoodia Cactus Keeps Men Alive*, THE OBSERVER (17 June 2001) teaches that *Hoodia gordonii* causes transient appetite suppression.

IV. Tamar KAHN, *Prickly Dispute Finally Laid To Rest*, BUSINESS DAY (JOHANNESBURG) (22 March 2002) teaches that *Hoodia gordonii* causes transient appetite suppression.

V. Orien Lee TULP *et al., Effect of Hoodia Plant on Food Intake and Body weight In Lean And Obese LA/Ntul//-cp Rats*, 15 FASEB JOURNAL A404 (7 March 2001) teaches that laboratory rats with impaired thermogenesis and sugar metabolism can lose weight when given *Hoodia gordonii*.

These references, alone or combined, fail to establish a *prima facie* case that it would have been obvious to use *Hoodia gordonii* for weight loss in humans.

B. Appetite Suppression Is Not Weight Control

The error in the Examiner's position appears based on a fundamental misunderstanding regarding the relationship between appetite suppression and weight control; while the Examiner equates the two, the art of record – and the Office's own records for other cases in this field – shows that one of skill in the art would recognize that the two concepts are not coterminous. To the contrary, one of skill in the art would understand that weight loss does not require appetite suppression, and appetite suppression does not of itself cause weight loss.

1. Weight Loss Does Not Require Appetite Suppression

It is possible to cause weight loss without suppressing appetite. This is the clinical result obtained by the use of amphetamines or exercise, both of which increase the user's rate of metabolizing calories, and both of which can thus cause weight loss even without a suppressed appetite. *See e.g.,* Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶ 9.

2. Appetite Suppression Does Not Always Cause Weight Loss

Similarly, it is possible to suppress appetite without causing weight loss. Apparently, suppressing food intake lowers the body's basal metabolic rate. *See* Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶ 10. This response allows the body to maintain a constant weight even with a lower caloric intake. *Id.*

The art of record confirms this. For example, VAN HEERDEN at Example 44 teaches that the appetite suppressant compound fenfluramine has no effect on body weight:

> "fenfluramine (7.5 mg/kg) produced statistically significant reductions in food consumption.... No statistically significant effects on water consumption or bodyweight were recorded."

Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶ 11 (quoting VAN HERDEN). Similarly, VAN HEERDEN teaches that the compound 3-0-[-β-

D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one suppresses appetite, yet has no effect on body weight:

> "Sample 3 (active moiety) produced statistically significant reductions in food consumption at an oral dose of 5.0 mg/kg. No statistically significant effects on body weights were produced by the active moiety."

Id. at ¶ 12. VAN HEERDEN thus confirms that appetite suppression does not cause weight loss; to the contrary, appetite suppression may have no effect on body weight. *Id.* at ¶¶ 8 to 46.

*3. Appetite Suppression May Cause Weight **Gain***

Appetite suppression does not invariably cause weight loss. To the contrary, it may cause weight ***gain***.

John BLUNDELL, 2 TRENDS IN PHARMACOL. SCI., 147 (1991), says that the most widely-used appetite suppressant in the world can also cause weight gain:

> "Food is an excellent anorectic agent which is known to reduce hunger and to suppress eating for some time after administration. However, one major disadvantageous side-effect of food as an appetite suppressant is that it is also known to lead to weight gain."

BLUNDELL thus concludes that appetite suppression is not sufficient for weight control; to the contrary, BLUNDELL concludes, "The development of safe and effective anti-obesity drugs involves far more than control of appetite; it includes

inter alia the intention to alter processes concerned with energy expenditure, fat synthesis and storage, and the digestion and absorption of nutrients."

An example of a compound which suppresses appetite, yet causes weight gain, is 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one, the active moiety studied in VAN HEERDEN. VAN HEERDEN's data shows that this compound suppresses appetite transiently, then stimulates appetite. Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶¶ 17 *et seq*. Apparently, the initial appetite suppression slows the user's metabolic rate, so the later appetite stimulation causes a marked *weight gain. Id.*

4. The Patent Office Recognizes That Appetite Suppression And Weight Loss Are Patentably Distinct Phenomena

One of skill in the art recognizes that appetite suppression and weight control are distinct phenomena. The Patent Office also recognizes this distinction. This is shown in the Office's processing of various third-party patents.

For example, Robert D. SOFIA, U.S. Patent No. 5,290,808 claims a method of administering 2-phenyl-1,3-propanediol dicarbamate to suppress appetite. In contrast, Walter E. KOZACHUK, U.S. Patent Nos. 5,942,540 and 6,515,019, claims the use of 2-phenyl-1,3-propanediol dicarbamate to treat obesity. Saliently, during prosecution of the '540 and '019 obesity patents, the Examiner

cited the '808 appetite suppression patent. The Office's ultimate decision to allow the obesity patents shows that the Office recognizes that one of skill in the art would know that treating obesity and suppressing appetite are not only different, but in fact are patentably distinct.

To render obvious, the prior art must teach each and every element of the claims at issue. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). In the immediate case, however, the references of record – alone nor combined – fail to teach every element of the claims.

C. VAN HEERDEN Fails To Teach Every Claim Element Of Claims 1, 3, 19 And 35

To establish *prima facie* obviousness, the prior art must teach each and every claim limitation. *E.g., In re Royka*, 490 F.2d 981 (C.C.P.A., 1974). In the immediate case, VAN HEERDEN fails to teach a number of claim limitations. To the contrary, VAN HEERDEN - alone nor combined - fails to teach each and every claim element of Claims 1, 3, 19 nor 35.

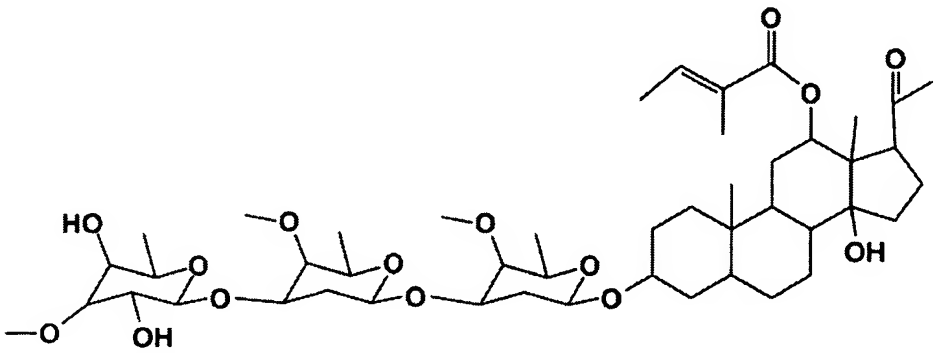
1. VAN HEERDEN Teaches That 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one Causes Weight Gain

To render the claims obvious, the prior art must teach a reasonable expectation of success. *E.g., In re Rinehart*, 531 F.2d 1048 (C.C.P.A., 1976). In

evaluating this, one must consider testimony which explains why the prior art fails to provide a reasonable expectation of success. *Amgen, Inc. v. Chugai Pharma. Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir., 1991), *certiorari denied*, 502 U.S. 856.

In the immediate case, the Inventor has testified at length and in detail about how VAN HEERDEN teaches a reasonable expectation not of success, but of *failure.*

In the immediate case, the claims are drawn to a method of weight loss using *Hoodia gordonii.* In contrast, VAN HEERDEN teaches that 3-0-[-β-D-thevetopyrano- sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one, (*see illustration*) a compound which occurs naturally in



Hoodia gordonii, can cause *weight gain. See* Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶¶ 17 *et seq.* While VAN HEERDEN does not address the use of *Hoodia gordonii* itself, VAN HEERDEN implies that the administration of *Hoodia gordonii* may entail the administration of a weight-gain inducing amount of 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-

tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one. VAN HEERDEN thus implies that the administration of *Hoodia gordonii* may cause weight gain.

This result is the opposite to the Inventor's result, and the opposite to the use claimed. VAN HEERDEN thus teaches a reasonable expectation of *failure*. VAN HEERDEN thus teaches away from the claimed invention.

2. VAN HEERDEN Teaches the use of 3-0-[-β-D-thevetopyranosylcymaro-pyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one, not Hoodia gordonii

VAN HEERDEN teaches the use of 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one. *See* Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶¶ 42 to 43. VAN HEERDEN does not teach nor claim a use of a plant. *Id.*

3. VAN HEERDEN Fails to Teach the Administration Regimen of Claim 2, nor of claim 35.

VAN HEERDEN fails to teach the administration regimen of Claim 2, nor of claim 35.

4. VAN HEERDEN Fails to Teach the Combination of Claim 3 Nor Claim 19

VAN HEERDEN fails to teach the combination of *Hoodia* with glucosamine, nor a stimulant, nor with any other claimed ingredient.

5. *VAN HEERDEN Fails to Render Obvious the Claimed invention*

VAN HEERDEN fails to render obvious the claimed invention because VAN HEERDEN fails to teach each element of the claims and because VAN HEERDEN teaches away from the claimed invention.

D. BARNETT and KAHN Fail to Teach Weight Loss

Anthony BARNETT, *In Africa the Hoodia Cactus Keeps Men Alive*, THE OBSERVER (17 June 2001) and Tamar KAHN, *Prickly Dispute Finally Laid To Rest*, BUSINESS DAY (JOHANNESBURG) (22 March 2002) each teach that *Hoodia gordonii* causes transient appetite suppression. *See* Albert M. Fleischner, Declaration (13 June 2006) at ¶¶ 32 to 33.

While each teaches appetite suppression, neither teaches that *Hoodia gordonii* can cause weight loss. *Id.* Neither teaches the claimed administration periods. Neither teaches the combination of *Hoodia* with glucosamine, nor a stimulant, nor with any other claimed ingredient.

E. HABECK Refuses To Say Whether Or Not 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one Causes Weight Loss

Martina HABECK, *A Succulent Cure To End Obesity*, 7 DRUG DISCOV. TODAY 280 (March, 2002) summarizes a corporate news release issued by Phytopharm, Ltd. of the United Kingdom. HABECK teaches that a study was

done of two groups of obese people. One group was given 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one; the other (control) group was not. Both groups were then confined for 15 days in prison-like conditions. *See* Albert M. Fleischner, Declaration (13 June 2006) at ¶¶ 25-26.

After 15 days, the group given 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one had reduced their body fat content by 1 kilogram. *Id.* HABECK fails to say, however, how much body fat the control group lost. *Id.* at ¶¶ 27-30. To the contrary, HABECK specifically withheld the results of the control group. *Id.*

HABECK therefore fails to inform one of skill in the art about whether the body fat change was due to, for example, the prison-like conditions under which test subjects were held, or the bad quality of food which they were given. This document therefore fails to inform one of skill in the art whether the change in body fat was caused by 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy- 14β-hydroxy-14-pregn-50-en-20-one, or by some other factor. *Id.*

Further, concealing control group results is unusual. *Id.* It implies that the experiment produced adverse data. *Id.* Thus, one of skill in the art would

read HABECK to imply that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one was not effective to reduce body fat. *Id.*

1. HABECK Fails to Teach the Administration Regimen of Claim 2, nor of claim 35.

HABECK Fails to Teach the Administration Regimen of Claim 2, nor of claim 35.

2. HABECK Fails to Teach the Combination of Claim 3 Nor Claim 19

HABECK fails to teach the combination of *Hoodia* with glucosamine nor a stimulant, nor with any other ingredient.

3. HABECK Is an Invitation To Experiment

Proposing that research be done, without providing an assurance of success, is a mere "invitation to experiment." *See Elan Pharma., Inc. v. Mayo Found. Med. Educ. And Res.,* 304 F.3d 1221, 1228 (Fed. Cir. 2002.

For example, in *Adang v. Fischoff*, 286 F.3d 1346, 1352 (Fed. Cir., 2002) the prior art reference taught that "the analysis was ongoing." The Federal Circuit found that where the prior art itself taught that the analysis was ongoing, rather than complete, the prior art merely provided an invitation to invent, not an enabling disclosure sufficient to render obvious the claims at issue.

Similarly, in *Hybritech Inc. v Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir., 1986), the Federal Circuit found that numerous prior art predictions of future success merely amounted to a collection of invitations to invent, rather than a disclosure enabling the practice of the claimed invention.[4] The court noted that because the prior art failed to provide an assurance of success, it did not render the claimed invention obvious.

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[4] *Hybritech* provides a number of examples of prior art references which invite experimentation. The inventor claimed the use of monospecific antibodies in immunodiagnostic testing. The references of record art taught, *inter alia*:

- ✓ "The use of monospecific antibodies in immunodiagnostic testing is obvious,"
- ✓ "The specificity and uniformity of monoclonal antibodies should markedly improve diagnostic accuracy,"
- ✓ "An essentially unlimited supply of monoclonal antibodies, precisely defined according to amount and affinity, will lead to major improvements and innovations in immuno medicine techniques."
- ✓ "For immunodiagnostics, monoclonal antibodies will improve performance, reduce costs and open up types of immunological testing. More obvious advances will include: antibodies for use with … enzyme … immunoassays,"
- ✓ "Combined with the exploitation of the in vitro hybridoma techniques of antibody production … with which large quantities of monospecific antibodies can be produced, the emergence of simple and reliable assay procedures … is within sight."

See Hybritech Inc. v Monoclonal Antibodies, Inc., 623 F.Supp. 1344, 1355 (N.D.Cal., 1985). The Federal Circuit found such teachings to be mere invitations to do research. *Hybritech Inc. v Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir., 1986).

In the instant case, HABECK teaches that it is still "early days" in doing research in this area. Albert M. Fleischner, Declaration (13 June 2006) at ¶ 31. HABECK teaches that for a useful invention to be made, further experimentation needs to be done to determine whether the effect is consistent over longer periods of time. *Id.* HABECK specifically teaches that for a useful invention to be made, further experimentation needs to be done to "take a closer look at the dosing interval." *Id.*

HABECK thus provides an invitation to experiment, with no assurance of success. *Id.*

F. TULP Provides an Invitation To Experiment

TULP (2001) fails to render the claims obvious because TULP (2001) presents results which are not indicative of efficacy in humans.

1. TULP's Results With LA//Ntul//-cp Mutant Laboratory Rats Do Not Predict Human Efficacy

TULP (2001) uses LA/Ntul//-cp laboratory rats. Albert M. Fleischner, Declaration (13 June 2006) at ¶¶ 17 to 22. LA/Ntul//-cp laboratory rats have a number of mutations. These mutations cause impaired carbohydrate tolerance, hyperamylinemia, hypertrigliceridimia and hypercholesterolemia, and an impaired capacity for non-shivering thermogenesis and energy expenditure. *Id.* These rats display morbid, early-onset obesity. *Id.* at ¶ 19.

TULP teaches that this kind of rat can lose weight if administered *Hoodia gordonii* for short periods. This result, however, fails to provide any assurance of success in humans because LA/Ntul//-cp mutants are so different from normal rats (and from normal human beings). Albert M. Fleischner, Declaration (13 June 2006) at ¶ 20 to 23. TULP's results do not provide any assurance of success in humans. Because TULP fails to teach an assurance of success, TULP provides a mere invitation to experiment.[5] *See Elan Pharma., Inc. v. Mayo Found. Med. Educ. And Res., 304 F.3d 1221, 1228 (Fed. Cir. 2002)*; *Adang v. Fischoff*, 286 F.3d 1346, 1352 (Fed. Cir., 2002); *Hybritech Inc. v Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir., 1986).

2. TULP Fails To Provide A Motivation To Modify Its Disclosure To Create The Combination Of Claims 3 And 19, Nor The Administration Regimens

The Examiner says that the claims differ from TULP in two aspects: TULP fails to teach the combination of claims 3 and 19, and TULP fails to teach the administration regimens of claims 2 and 35.

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[5] TULP (2001) also says that *Hoodia* extract changes food intake. Albert M. Fleischner, Declaration (13 June 2006) at ¶¶ 10-16. TULP (2001), however, fails to say *how much* food intake changes. *Id.* This leaves one to speculate whether his *Hoodia* extract causes a net decrease or ***a net increase*** in food intake. *Id.* at ¶ 15.

a) The Art Of Record Fails To Suggest the Administration Periods Of Claims 2 and 35

A *prima facie* case of obviousness requires identification in the prior art of record of some suggestion to modify the prior art to reach the claimed invention. *In re Lee*, 277 F.3d 1338, 1344 (Fed.Cir., 2002) (there must be some "hint or suggestion in a particular reference").

In the immediate case, the OFFICE ACTION fails to identify any suggestion in the art of record to make the claimed combinations or the claimed administration regimens. The OFFICE ACTION simply takes judicial notice that "determining appropriate, suitable time periods and intervals ... is deemed merely a matter of judicious selection and routine optimization."

Applicant respectfully disagrees because HABECK, at page 2, expressly teaches that determining appropriate administration intervals is neither routine nor predictable. *See* Albert M. FLEISCHNER, Declaration (13 June 2006) at ¶ 31.

Furthermore, the art of record teaches that at whatever interval, the claimed invention would not work. For example, VAN HEERDEN at Figures 5 and 6 shows that administration would precipitate weight ***gain***, not weight loss. *See* Albert M. Fleischner, Declaration (30 Dec 2005) at ¶ 17 *et seq*. Similarly, HABECK teaches that administration does not produce weight ***loss***, and may

produce weight ***gain***. *See* Albert M. Fleischner, Declaration (13 June 2006) at ¶¶ 15, 28-30, 35-36.

b) The Art Of Record Fails to Suggest the Combination of Claims 3 and 19

The OFFICE ACTION correctly notes that it is *prima facie* obvious to combine ingredients which are each individually recognized as effective for the same use. The OFFICE ACTION then alleges that *Hoodia gordonii* has a "well recognized activity in promoting weight loss" in humans.

This allegation is not correct. To the contrary, VAN HEERDEN at Figures 5 and 6 teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one has "well recognized activity" in promoting weight ***gain*** in humans. *See* Albert M. Fleischner, Declaration (30 Dec 2005) at ¶ 17 *et seq*.

Similarly, HABECK at 1 teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one has no "well recognized activity"; to the contrary, it might promote weight gain in humans, but the relevant data has been withheld from the public. *See* Albert M. Fleischner, Declaration (13 June 2006) at ¶¶ 15, 30, 34-36.

Thus, it would not have been obvious to combine *Hoodia gordonii* with a stimulant, nor with glucosamine.

IV. THE CLAIMED INVENTION SHOWS SECONDARY INDICIA OF NON-OBVIOUSNESS

The claimed invention has several secondary indicia of non-obviousness. These include A. unexpectedly successful results, B. achieving a new and different function, and C. widespread copying by competitors.

A. The Inventor has achieved unexpected success

Tthe inventor has shown that *Hoodia gordonii* is effective for weight loss. *See* Albert M. FLEISCHNER, DECLARATION (21 December 2005) at ¶¶ 47 to 56, and the Exhibits (clinical trial results) appended to that DECLARATION.

The inventor's results would not have been expected by one of skill in the art at the time the inventor made his invention. *Id.* at ¶ 57. Rather, VAN HEERDEN at Figures 5 and 6 teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one causes weight gain.

There is a nexus between the inventor's scientific results and the pending patent claims, because the Inventor's actual clinical testing results discussed in his 2005 Declaration would be considered by one of skill in the art to have probative value in showing that the pending patent claims are both enabled and non-obvious. *Id.* at ¶ 58 to 59.

B. The inventor has achieved a new or different function

While not required for non-obviousness, achieving a new or different function indicates the claimed invention is non-obvious. *See Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, *rehearing denied*, 426 U.S. 955 (1976); *Anderson's Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57 (1969).

In the immediate case, the inventor has achieved a function which is not only different from the prior art, but the direct opposite of it. The prior art teaches that 3-0-[-β-D-thevetopyrano-sylcymaropyranosyl]-12β-0-tigloyloxy-14β-hydroxy-14-pregn-50-en-20-one increases body mass. In contrast, the Inventor claims methods to *decrease* body mass using *Hoodia gordonii* itself.

The claimed invention is non- obvious because the Inventor has achieved a function different than that taught by the prior art.

C. The claimed invention is being widely copied

Widespread copying is a secondary indicator of non-obviousness. *See Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675 (Fed. Cir., 1988).

In the immediate case, the claimed invention is being widely copied. This is shown in two places in the record.

First, quite soon after the Applicant began offering for sale its TrimSpa® brand *Hoodia gordonii* weight control product, competitors began selling slavish copies of it. These copies, sold as TrimSmart™, TrimClub™ and

HoodiaSpa™, copied the original TrimSpa® product, the TrimSpa® formula, and used trade marks and trade dress deceptively similar to the original TrimSpa® packaging. *See* PETITION TO MAKE EXAMINATION SPECIAL PURSUANT TO M.P.E.P. § 708.02 (II) (6 July 2005). On reviewing this evidence, the Office agreed that it shows unauthorized copying. *See* ORDER GRANTING PETITION TO MAKE EXAMINATION SPECIAL (2 August 2005).

Second, since its commercial launch, Applicant's TrimSpa® brand *Hoodia gordonii* weight control product has enjoyed significant and continued commercial success. This success has, unfortunately, prompted additional copying, copying which is not merely widespread, but endemic.

For example, with the Google™ search engine, an internet search made on 7 May 2006 and using the search term "hoodia" identified a large number of sources advertising *Hoodia* weight loss products for sale in The United States. These competitors include www.hoodoba.com, www.weightlossguide.com, www.h57.com, www.hoodithin.com and www.phenterlean.com. *See* INFORMATION DISCLOSURE STATEMENT (8 May 2006). While these products no longer copy Applicant's TrimSpa® trade mark, they continue to copy the Inventor's claimed invention. On information and belief, each of these products

was made after the TrimSpa® product achieved commercial success, and each of these products appears specifically designed to pirate the claimed invention.

Applicant concedes that none of these competitors appears at present to be particularly large; to the contrary, they appear to be quite small, little more than individuals operating email spam software out of a personal residence. Nonetheless, "widespread copying" does not require the copier be large nor well-financed. This evidence of widespread copying therefore indicates that the claimed invention is non-obvious. *See Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675 (Fed. Cir., 1988).

V. CONCLUSION

The OFFICE ACTION fails to state a *prima facie* case to reject any claim. Applicant therefore respectfully requests withdraw of all rejections and prompt allowance of its claims.

Respectfully Submitted on behalf of the Applicant by its attorneys,
PHARMACEUTICAL PATENT ATTORNEYS, LLC

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Wednesday, July 05, 2006

SD:\TrimSpa\10.693,442 Appeal Brief (May 2006).doc

A. CLAIMS APPENDIX

1. A method of body weight reduction, comprising administering to a human in need thereof a body weight reducing amount of *hoodia gordonii* at least once every about 48 hours, for at least about 45 days.

2. The method of claim 1, said *hoodia gordonii* administered at least three times every 24 hours.

3. The method of claim 1, further comprising administering a second compound selected from the group consisting of a stimulant and glucosamine, said second compound administered in an amount sufficient to lessen the amount of *hoodia gordonii* required for body weight reduction.

4. The method of claim 3, said second compound comprising a stimulant and glucosamine.

5. The method of claim 4, said *hoodia gordonii* present in an amount from about 5 to about 200 milligrams per day, said glucosamine present in an amount from 0 to about 200 milligrams per day, and said stimulant comprising caffeine present in an amount from 0 to about 250 milligrams per day.

6. The method of claim 3, wherein said *hoodia gordonii* consists essentially of the whole *hoodia gordonii* plant, less the roots.

7. The method of claim 2, comprising administering from about 5 to about 200 milligrams of *hoodia gordonii*, together with from about 50 to about 200 micrograms of chromium, from about 10 to about 50 micrograms of vanadium, 0 to about 400 milligrams of glucomannan, from about 25 to about 200 milligrams of sodium carboxymethylcellulose, 0 to about 15 milligrams of citrus naringinine, 0 to about 200 milligrams of glucosamine, 0 to about 500 milligrams of cocoa PEA standardized extract, and 0 to about 250 milligrams of green tea extract.

8. to 16. (cancelled)

17. The method of claim 2, comprising administering from about 5 to about 200 milligrams of *hoodia gordonii*, together with from about 50 to about 200 micrograms of chromium, from about 10 to about 50 micrograms of vanadium, from 0 to about 200 milligrams of sodium carboxymethylcellulose, 0 to about 15 milligrams of citrus naringinine, 0 to about 100 milligrams of glucosamine, 0 to about 500 milligrams of cocoa PEA standardized extract, 0 to about 250 milligrams of green tea extract, from about 10 to about 200 milligrams of 3-acetyl-7-oxo-dehydroepiandrosterone, and 0 to about 15 milligram of ma huang .

18. The method of claim 2, comprising administering from about 5 to about 200 milligrams of *hoodia gordonii*, together with from about 50 to about 200 micrograms of chromium, from about 10 to about 50 micrograms of vanadium,

from 0 to about 200 milligrams of sodium carboxymethylcellulose, 0 to about 15 milligrams of citrus naringinine, 0 to about 500 milligrams of cocoa PEA standardized extract, 0 to about 250 milligrams of green tea extract, and 0 to about 250 milligrams of *Coleus Forskohlii*.

19. A composition of matter for body weight reduction, comprising a body weight reducing amount of *hoodia gordonii* together with a second compound selected from the group consisting of a stimulant and glucosamine, said second compound in an amount sufficient to lessen the amount of *hoodia gordonii* required for body weight reduction.

20. The composition of claim 19, said second compound comprising a stimulant and glucosamine.

21. The composition of claim 19, said *hoodia gordonii* present in an amount from about 5 to about 200 milligrams, said glucosamine present in an amount from 0 to about 200 milligrams, and said stimulant comprising caffeine present in an amount from 0 to about 250 milligrams.

22. The composition of claim 19, wherein said *hoodia gordonii* consists essentially of the whole *hoodia gordonii* plant, less the roots.

23. The composition of claim 19, said *hoodia gordonii* comprising from about 5 to about 200 milligrams of *hoodia gordonii* and said stimulant comprising green tea extract.

24. The composition of claim 23, said *hoodia gordonii* comprising about 100 milligrams of *hoodia gordonii* and said stimulant comprising about 250 milligrams of green tea extract.

25. The composition of claim 24, further comprising about 75 micrograms of chromium, about 15 micrograms of vanadium, and about 100 milligrams of sodium carboxymethylcellulose, and about 7.5 milligrams of citrus naringinine.

26. The composition of claim 19, said *hoodia gordonii* comprising about 100 milligrams of *hoodia gordonii* and said stimulant comprising cocoa PEA standardized extract.

27. (canceled)

28. The composition of claim 19, said *hoodia gordonii* comprising about 150 milligrams of *hoodia gordonii* and said second compound comprising glucosamine.

29. The composition of claim 28, further comprising cocoa PEA standardized extract, and green tea extract.

30. The composition of claim 23, said *hoodia gordonii* comprising about 7.5 milligrams of *hoodia gordonii* , said stimulant further comprising cocoa PEA standardized extract.

31. The composition of claim 23, said *hoodia gordonii* comprising about 100 milligrams of *hoodia gordonii* and said second compound comprising about 75 micrograms of chromium, about 15 micrograms of vanadium, and about 50 milligrams of sodium carboxymethylcellulose; said composition further comprising about 200 milligrams of glucomannan, about 5 milligrams of citrus naringinine, about 50 milligrams of glucosamine, about 162.5 milligrams of cocoa PEA standardized extract, and about 125 milligrams of green tea extract.

32. The composition of claim 30, said stimulant comprising about 162.5 milligrams of cocoa PEA standardized extract and about 125 milligrams of green tea extract.

33. The composition of claim 19, said stimulant comprising *ma huang*.

34. The composition of claim 19, further comprising *Coleus Forskohlii*.

35. A method of body weight reduction, comprising administering to a human in need thereof *hoodia gordonii* in an amount sufficient to suppress the appetite after said administration, said administration repeated a plurality of times, each one of

said times occurring before said *hoodia gordonii* causes an appetite stimulating effect.

36. The method of claim 35, said *hoodia gordonii* administered at least three times every 24 hours.

37. The method of claim 35, further comprising administering a second compound selected from the group consisting of a stimulant and glucosamine, said second compound administered in an amount sufficient to lessen the amount of *hoodia gordonii* required for body weight reduction.

38. The method of claim 37, said second compound comprising a stimulant and glucosamine.

39. The method of claim 38, said *hoodia gordonii* present in an amount from about 5 to about 200 milligrams per day, said glucosamine present in an amount from 0 to about 200 milligrams per day, and said stimulant comprising caffeine present in an amount from 0 to about 250 milligrams per day.

40. The method of claim 37, wherein said *hoodia gordonii* consists essentially of the whole *hoodia gordonii* plant, less the roots.

B. EVIDENCE APPENDIX

Enclosed find the two Rule 132 Declarations of record in this case. All evidence relied on has previously been entered into the record before filing of the NOTICE OF APPEAL, as shown on the table below. Physical copies of this evidence is not included here because the Board has copies of this evidence already, via the PAIR system.

Evidence	Date Entered Into Record
T.H. ARNOLD, Medicinal and Magival Plants, pp. 170-71 (2002)	13 June 2006
Anthony BARNETT, *In Africa the Hoodia Cactus Keeps Men Alive*, THE OBSERVER (17 June 2001)	6 Feb 2006
John BLUNDELL, *Pharmacological Approaches to Appetite Suppression*, 12 Trends in Pharmacol. Sci. 147 (1991)	13 June 2006
Richard COWLING, *Namaqualand: A Succulent Desert* (2003)	13 June 2006
Albert M. FLEISCHNER, DECLARATION (21 Dec. 2005)	30 Dec 2005
Albert M. FLEISCHNER, DECLARATION (10 May 2006)	13 June 2006
Google, Inc., *Search Results For the Term "Hoodia"* (7 May 2006)	9 May 2006
www.H57com website	9 May 2006
Martina HABECK, *A Succulent Cure To End Obesity*, 7 DRUG DISCOV. TODAY 280 (March, 2002)	6 Feb 2006
www.Hoodithin.com website	9 May 2006
www.hoodia-dietpills.com	9 May 2006

www.Hoodoba.com website	9 May 2006
Laura JOHANNES, *Aches & Claims: Hoodia's Hunger Claims*, Wall Street Journal (2005)	27 Dec 2005
Judith KORNER, *Effects of Leptin Receptor Mutation...*, 141 Endocrinology 2465 (2000)	13 June 2006
Tamar KAHN, *Prickly Dispute Finally Laid To Rest*, BUSINESS DAY (JOHANNESBURG) (22 March 2002)	6 Feb 2006
Tom MANGOLD, *Magic Molecule*, THE AGE (Australia) Section A3, page 6 (23 June 2003)	13 June 2006
Ian B. OLIVER, Grow Succulents	9 May 2006
www.Phenterlean.com website	9 May 2006
TrimSpa Corporation, PETITION TO MAKE EXAMINATION SPECIAL (July 2005)	13 July 2005
Orien Lee TULP *et al., Animal Model: Metabolic and Thermic Responses to Diet and Environment (4° C) in Obesity During Aging In the LA/Ntul//-cp Rat*, 1 NESTLE NUTRITION WORKSHOP SERIES: CLINICAL AND PERFORMANCE PROGRAMME 149 (Basel, 1999)	13 June 2006
Orien Lee TULP *et al., Effect of Hoodia Plant on Food Intake and Body weight In Lean And Obese LA/Ntul//-cp Rats*, 15 FASEB JOURNAL A404 (7 March 2001) (abstract only)	23 Oct 2003
Pieter VAN DER WALT, *The Kalahari and Its Plants* (1999)	13 June 2006
Fanie Retief VAN HEERDEN *et al., Pharmaceutical Compositions Having Appetite Suppressant Activity*, U.S. Letters Patent No. 6,376,657	23 Oct 2003
Ben-Erik VAN WYK, *People's Plants* (2000)	13 June 2006
www.Weightlossguide.com website	9 May 2006

In The United States Patent Office

In re Albert M. FLEISCHNER, Ph.D., "Herbal Composition for Weight Control"	Serial No. 10/693,442 Filed 23 October 2003

RULE 132 DECLARATION

I, Albert M. Fleischner, Ph.D., do hereby swear as follows:

1) I received a Bachelors of Science in Pharmacy in 1963 from Temple University, Philadelphia, Pennsylvania. I received a Masters of Science in Pharmaceutical Science in 1970 from Rutgers University, New Brunswick, New Jersey. I received a Doctorate in Philosophy in Pharmaceutical Sciences in 1976 from Rutgers University, New Brunswick, New Jersey.

2) After receiving my Doctorate in Philosophy, I worked as a Group Leader in Personal Care and OTC Products at the Lehn & Fink division of Sterling Drug

Corporation; as the Manager of Technical Services for Amerchol Inc.; as a pharmaceutical manufacturing process development scientist at Schering Plough R&D; as the Director of Technical Service at International Sourcing, Incorporated; as the Director of Pharmaceutics at Roberts Pharmaceutical, Inc.; and as the Vice President of Manufacturing and Research & Development at Bradley Pharmaceutical.

3) I currently am the Chief Scientific Officer of the assignee for the captioned patent application. As such, I am responsible for, among other things, developing dietary supplement formulations and assessing the clinical support for dietary supplement labeling claims.

4) I am the inventor of record of United States Letters Patent No. 6,420,350, United States Published Patent Application No. 2002/0136781, and several others. I am the inventor of record of one of the references which is cited against the immediate application.

5) I therefore respectfully believe that I am one of skill in the art.

6) I have reviewed the art of record in this case, including Fanie Retief VAN HEERDEN *et al., Pharmaceutical Compositions Having Appetite Suppressant Activity*, U.S. LETTERS PATENT NO. 6,376,657; Orien Lee TULP *et al., Effect Of Hoodia Plant on Food Intake and Body Weight In Lean and Obese LA/Ntul//-cp*

Rats, 15 FASEB JOURNAL A404 (March 7, 2001) (Abstract only) ("TULP 2001"); Martina HABECK, *A Succulent Cure To End Obesity*, 7 DRUG DISCOVERY TODAY 280 (March, 2002); Tamar KAHN, *Prickly Dispute Finally Laid To Rest*, BUSINESS DAY (Johannesburg) (22 March 2002); Janice LIMSON, *Focus On Biopiracy In Africa*, SCIENCE IN AFRICA (September 2002); WIMSA, *San Rights Vis-à-vis The Hoodia Succulent*, WIMSA REPORT ON ACTIVITIES (2003); Jen CULLY, *African Hoodia Gordonii Plant May Help Fight Fat* (21 Nov. 2004); Anthony BARNETT, *In Africa the Hoodia Cactus Keeps Men Alive*, THE OBSERVER (17 June 2001); and *Phytopharm Boosts P57 Production*, MARKET LETTER (10 December 2001).

7) I have also reviewed the OFFICE ACTION dated 10 February 2006. I respectfully disagree with the Examiner's characterization of much of the aforementioned prior art. I infer that much of the Examiner's misunderstanding regarding the art of record is based on the fact that this art is largely drawn not from peer-reviewed scientific literature, but from meeting announcements, corporate publicity releases and newspaper summaries.

Jen CULLY

8) Regarding Jen CULLY, *African Hoodia Gordonii Plant May Help Fight Fat* (21 Nov. 2004), the OFFICE ACTION at page 4 says:

> the only place in the world where *Hoodia gordonii* grows is in South Africa – e.g., this cactus plant only grows wild in the Kalahari

> Desert.... it is not apparent if the plant is readily available to the public.

I respectfully disagree. *Hoodia gordonii* does indeed grow wild in the Kalahari Desert, along a range lying in South Africa and in the adjoining nation of Namibia. This is not, however, "the only place in the world" where the plant grown. Rather, the botanical literature discussing Hoodia does not identify any reason why this cactus could not be cultivated in any similar arid environment. *See e.g.*, Pieter VAN DER WANT *et al.*, THE KALAHARI AND ITS PLANTS at 85 (1999); T.H. ARNOLD *et al.*, MEDICINAL AND MAGICAL PLANTS OF SOUTHERN AFRICA at 170-71 (Stelitzia Ltd., publ., 2002); Ben-Erik VAN WYK *et al.*, PEOPLE'S PLANTS: A GUIDE TO USEFUL PLANTS OF SOUTHERN AFRICA at 63, 70-71, 74 (2000); Richard COWLING *et al.*, NAMAQUALAND, A SUCCULENT DESERT at 39-51 (Botanical Soc. of South Africa, publ., 1999). For the convenience of the Examiner, I enclose copies of each of these references.

9) This is confirmed by current practice in the industry. For example, I see no reason that this cactus could not be cultivated, as are many other types of cacti, in a non-desert location in a greenhouse; for example, I understand that *Hoodia gordonii* is now cultivated in The United Kingdom.

Orien Lee TULP *et al.* ("TULP 2001")

10) Regarding Orien Lee TULP *et al., Effect Of Hoodia Plant on Food Intake and Body Weight In Lean and Obese LA/Ntul//-cp Rats*, 15 FASEB JOURNAL A404 (March 7, 2001) (Abstract only) ("TULP 2001"), the OFFICE ACTION at page 8 says:

> Tulp et al. beneficially teach that a ground-up slurry of *Hoodia gordonii* plant effectively decreased the body weight of obese rats and hat the results of this study indicate that orally administered *Hoodia Gordonii* has strong potential for clinical appetite regulation and weight control.

I respectfully disagree with certain of the facts asserted or implied by this statement.

One Of Skill In The Art Would Read TULP 2001 To Conceal His Actual Results Regarding Appetite Suppression

11) One of skill in the art would read TULP 2001 to teach that certain amounts of *Hoodia sp.* extract or aqueous slurry cause appetite suppression in 50% of the laboratory rats tested. TULP says, "The ED50 for appetite suppression in a 4 h feeding test ranged from 1.8 to 2.7 g/kgBW/rat for the various Hoodia sp, and were similar in both lean and obese phenotypes."

12) TULP is, however, pointedly vague in disclosing *how much* appetite suppression is caused. TULP says,

> "Spontaneous FI [food intake] decreased by < 50% within 2h of administration of crude plant mixture or extract."

One of skill in the art would read this to teach that within two hours after administration of Hoodia, food intake decreased by less than 50%.

13) How much less, however, is left to speculation. For example, food intake might have decreased by 49%; that is, food intake might have decreased to 100% - 49% = 51% of the pre-administration level food intake level, a significant decrease.

14) Alternatively, food intake might have decreased by 10%, leaving food intake at 90% of the pre-administration level food intake level. For a 2 hour period for laboratory rats, this would be a statistically-insignificant change in food intake.

15) Alternatively, TULP might have observed a food intake decrease of less than 0% – that is, a net ***increase*** in food intake.

16) TULP 2001 is an Abstract of a conference presentation. As such, it does not purport to provide a full and candid disclosure of the researchers' results. Rather, it merely provides an enticing hint of the potential contents of that presentation, enticing the reader to attend that presentation and find out more about the researchers' results. The Abstract itself, however, pointedly conceals whether *Hoodia* causes a net increase or decrease in food intake.

TULP (2001) Investigates Rats Genetically Bred To Have Abnormal Body Mass and An Abnormal Relationship Between Body Mass and Food Intake

17) It is known in the art to use laboratory rats with any of a variety of genetic mutations which provide "uniquely different metabolic characteristics including diabetes (NIDDM), atherosclerotic traits, renal dysfunction, and congestive heart failure." *See* Orien Lee TULP *et al., Animal Model: Metabolic and Thermic Responses To Diet and Environment (4° C) In Obesity During Aging In the LA/Ntul//-cp Rat*, 1 NESTLÉ NUTRITION SERIES: CLINICAL & PERFORMANCE PROGRAMME 149, 150 (Karger AG, Basel, publ., 1999) ("TULP (1999)").

18) TULP (2001) teaches results obtained in LA/Ntul//-cp laboratory rats. The LA/Ntul//-cp rat is a rat with a specific constellation of genetic mutations. *Id.* This constellation of genetic mutations impart "marked obesity, impaired carbohydrate tolerance, hyperamylinemia, hypertrigliceridimia and hypercholesterolemia, and an impaired capacity for nonshivering thermogenesis (NST) and energy expenditure." *Id.* at 149.

19) Therefore, it is known in the art that LA/Ntul//-cp rats have an abnormal sugar metabolism and an abnormal relationship between body mass and food intake. TULP (2001) teaches that this relationship is, however, highly variable, so an individual LA/Ntul//-cp rat could be obese or could be lean, or could be

something in between. TULP (2001) at AB line 4 thus teaches to use both "lean and obese" phenotypes.

20) Given the effects of this constellation of mutations on body weight and metabolism, one of skill in the art would understand that results obtained with LA/Ntul//-cp laboratory animals would not necessarily correlate into an equivalent result in humans, or at least not in humans not carrying the same constellation of genetic mutations.

21) This is confirmed by TULP (2001). In summarizing their results, TULP (2001) does not conclude that *Hoodia* is effective for weight control in humans. Rather, TULP (at AB line 26-27) concludes: "These results indicate that Hoodia sp. may have strong potential for clinical appetite regulation and weight control." One of skill in the art would not read this to say that TULP teaches that *Hoodia sp.* is effective for human weight control. Rather, one of skill in the art would read this as an invitation to pursue further experimentation (in non-mutant rats, for example, or in humans) to determine whether or not *Hoodia sp.* may be effective for human weight control.

22) This conclusion is to be expected because Orien Lee TULP, being one of skill in the art, would not assume that the results obtained with LA//Ntul//-cp laboratory rats would show efficacy in humans.

23) I respectfully believe that my interpretation of TULP (2001) is corroborated by extrinsic evidence of product marketing. As part of my professional duties, I attempt to remain aware of the new products in this industry. I know of no product with a weight-control effective amount of *Hoodia gordonii* which was launched contemporaneously with, nor shortly after, the March, 2001 publication of TULP (2001). In contrast, shortly after the assignee of my patent launched its TrimSpa® brand hoodia product, this product was widely copied (*e.g.*, by TrimClub™, TrimSmart™ and HoodiaSpa™).

Fanie Retief VAN HEERDEN *et al.*

24) In my earlier DECLARATION, I say that the difference between "appetite suppression" and "weight loss" is known in the art. I add here John BLUNDELL, *Pharmacological Approaches To Appetite Suppression*, 12 TRENDS IN PHARMACOLOGICAL SCIENCES 147 (1991) (copy attached), which confirms this:

> Food is an excellent anorexic agent which is known to reduce hunger and to suppress eating for some time after administration. However, one major disadvantageous side-effect of food as an appetite suppressant is that it is also known to lead to weigh gain. ... The development of safe and effective anti-obesity drugs involves far more than control of appetite; it includes *inter alia* the intention to alter processes concerned with energy expenditure, fat synthesis and storage, and the digestion and absorption of nutrients.

I respectfully believe that this confirms that appetite suppression and weight loss are not equivalent concepts.

Martina HABECK

25) Regarding Martina HABECK, *A Succulent Cure To End Obesity*, 7 DRUG DISCOVERY TODAY 280 (March, 2002), the OFFICE ACTION says:

> Habeck also beneficially teaches that the cactus plant Hoodia gordonii (and extracts thereof) is well known to be useful as an anti-obesity agent

I respectfully disagree with the Examiner's characterization of this reference.

26) HABECK (at page 280, column 3) summarizes a December 2001 corporate news release announcing the completion of the third phase of a proof-of-principle study in humans. HABECK says:

> In the third phase, they moved on to investigate the effects on calorie intake in 19 overweight men who took the compound or placebo twice daily for 15 days. By the end of the study, men in the treatment group achieved a 30% reduction in calorie intake, accompanied by a significant reduction in body fat content by 1 kg. Dixey says, "this was a very demanding clinical study because people had nothing to do but eat and watch TV. To get an appetite suppressant to work in such an environment was very impressive and it shows how potent this drug is."

What HABECK does not say about this study, however, is at least as important as what HABECK does say.

27) First, HABECK fails to say that the study placed the test subjects in a phase-1 unit under "prison-like" conditions. In discussing the same third phase study discussed in HABECK, an Australian newspaper (THE AGE) noted:

> When the first human clinical trial was conducted by Phytopharm, the company chose a morbidly obese group of people from Leicester England, and placed them in a "phase 1 unit", a place as close to prison as it gets. All the volunteers could do was read papers and watch television – and eat. ... At the end of 15 days, the group on Hoodia had reduced their food intake by 1000 calories a day.

See Tom MANGOLD, *Magic Molecule* THE AGE (Australia) (23 June 2003) at Section A3, page 6. (I enclose a printout of this article. As the printout is legible with difficulty, I also append the full text of this article).

28) One of skill in the art reading the description of the third-phase study given in HABECK (or in MANGOLD) would question whether the body fat loss experienced by the *Hoodia*-administered test subjects was due to *Hoodia*, or due simply to holding the test subjects in prison-like conditions.

29) Determining this would require comparing the results seen in the *Hoodia*-administered test subjects to the results seen in the control group. The company which actually performed the study (Phytopharm, Ltd. of the United Kingdom), however, has refused to publish the results observed in the control group. *Cf.* HABECK (discussing only the results observed in "the treatment group"); MANGOLD (same). This omission makes it impossible for one of skill in the art to accurately ascertain whether the body fat loss was unique to the treatment group or was common to all test subjects.

30) One of skill in the art would recognize this omission of control group results as highly unusual. One of skill in the art would also read HABECK to conceal data necessary to correctly assess the third-phase test discussed. One of skill in the art would therefore likely read HABECK to imply that because the control group data had been concealed, that data is adverse (that is, that the control group results show no body fat loss caused by the tested *Hoodia* extract). One of skill in the art would therefore read HABECK (and MANGOLD) to: (A) fail to teach that *Hoodia* extract causes weight loss; and (b) imply that the *Hoodia* extract ***does not*** cause weight loss.

31) One of skill in the art would read HABECK to merely invite further experimentation. HABECK itself corroborates my interpretation. HABECK quotes Susan Jebb of the Medical Research Council (Cambridge, United Kingdom):

> Susan Jebb ... agrees that the results of the proof-of-principle study are very encouraging. However, she stresses that it is early days. "The studies they have done so far are only up to two weeks long. Now, they have to do longer studies in more people to demonstrate that this is a consistent effect. Obesity is a chronic relapsing problem and you need a treatment that is going to work safely and effectively over much longer periods of time."
>
> Dixey says their next step will be to take a closer look at the dosing interval and other pharmacodynamic parameters.

Susan Jebb confirms that as of March 2002, it was still "*early days*" in the research towards the claimed invention. Susan Jebb confirms that short-term (up to two week) studies *do not* predict a *consistent* effect, nor do they predict effectiveness in *long-term* use. One of skill in the art would therefore read HABECK to invite further experimentation, not teach the claimed invention.

Anthony BARNETT

32) Regarding Anthony BARNETT, *In Africa the Hoodia Cactus Keeps Men Alive*, THE OBSERVER (17 June 2001), the Examiner says:

> Barnett also beneficially teaches that the cactus plant *Hoodia gordonii* (and extracts thereof) is well known to be useful as an anti-obesity agent (see entire 3 page document).

I respectfully disagree with the Examiner's characterization of BARNETT. BARNETT at page 1, line 1, teaches that "African tribesmen have eaten the Hoodia cactus to stave off hunger and thirst on long hunting trips." In so doing, BARNETT teaches no more than does the prior art I discuss in my Specification. The remainder of BARNETT is not germane to my patent claims.

Tamar KAHN

33) Regarding Tamar KAHN, *Prickly Dispute Finally Laid To Rest*, BUSINESS DAY (Johannesburg) (22 March 2002), the Examiner says:

> Kahn also beneficially teaches that the cactus plant *Hoodia gordonii* (and extracts thereof) is well known to be useful as an anti-obesity agent (see entire 4 page document).

I respectfully disagree with the Examiner's characterization of KAHN. KAHN at page 1 teaches that "the San have used the Hoodia cactus as an appetite suppressant and thirst quencher." In so doing, KAHN teaches no more than does the prior art I discuss in my Specification. The remainder of KAHN is not germane to my patent claims.

The Examiner's Proposed Rationale to Modify the Prior Art

34) I respectfully believe that the foregoing prior art fails to support – and indeed even contradicts - the Examiner's proposed rationale to modify the prior art to make the claimed invention. As rationale, the Examiner says:

> It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made [to] repeatedly administer a weight-reducing amount of *Hoodia gordonii* to an obese and/or overweight subject, based upon the beneficial teachings of each of the cited references with respect to its well recognized activity in promoting weight loss and / or acting as an anti-obesity agent. The adjustment of particular conventional working conditions – e.g., determining appropriate, suitable time periods and intervals for orally administering such a Hoodia gordonii weight loss product – is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

I respectfully disagree.

35) First, the Examiner asserts that the art of record shows that *Hoodia gordonii* is "well recognized activity in promoting weight loss and / or acting as an anti-obesity agent." This is incorrect. As explained in my previous DECLARATION, some of the prior art of record shows that *Hoodia gordonii* had "well-recognized activity" in promoting weight ***gain***, not weight loss. Some of the newly-raised art of record corroborates this; for example, as discussed above, HABECK implies that *Hoodia gordonii* extract ***is not effective*** for weight loss.

36) Alternatively, some of the newly raised art (BARNETT, KAHN) teaches appetite suppression; as explained in my previous DECLARATION, appetite suppression is not weight loss. No art of record teaches that *Hoodia gordonii* is effective for human weight loss or as a human anti-obesity agent. The art of record therefore fails to support the Examiner's assertion that *Hoodia gordonii* is "well recognized activity in promoting weight loss and / or acting as an anti-obesity agent."

37) Second, the Examiner asserts that "determining appropriate, suitable time periods and intervals for orally administering such a *Hoodia gordonii* weight loss product – is deemed merely a matter of judicious selection and routine optimization." The Examiner's assertion is contradicted by the art of record. HABECK, for example, expressly teaches that two week dosing intervals do not

demonstrate a consistent effect, nor that *Hoodia* is safe and effective when administered over longer periods of time. HABECK also teaches that given the prior art at the time, those of skill in the art needed "to take a closer look at the dosing interval" before arriving at an operable invention. I therefore respectfully believe that the prior art shows that finding an effective dosing interval represents more than "routine optimization."

Summary

39) In view of the foregoing, I respectfully believe that my pending patent claims are not obvious in light of the art of record.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

Albert M. Fleischner

Albert M. FLEISCHNER, Ph.D.

Dated as of 10 March 2006

IN THE UNITED STATES PATENT OFFICE

In re Albert M. FLEISCHNER, Ph.D., "Herbal Composition for Weight Control"	Serial No. 10/693,442 Filed 23 October 2003

RULE 132 DECLARATION

I, Albert M. Fleischner, Ph.D., do hereby swear as follows:

1) I received a Bachelors of Science in Pharmacy in 1963 from Temple University, Philadelphia, Pennsylvania. I received a Masters of Science in Pharmaceutical Science in 1970 from Rutgers University, New Brunswick, New Jersey. I received a Doctorate in Philosophy in Pharmaceutical Sciences in 1976 from Rutgers University, New Brunswick, New Jersey.

2) After receiving my Doctorate in Philosophy, I worked as a Group Leader in Personal Care and OTC Products at the Lehn & Fink division of Sterling Drug Corporation; as the Manager of Technical Services for Amerchol Inc.; as a pharmaceutical manufacturing process development scientist at Schering Plough R&D; as the Director of Technical Service at International Sourcing, Incorporated; as the Director of Pharmaceutics at Roberts Pharmaceutical, Inc.; and as the Vice President of Manufacturing and Research & Development at Bradley Pharmaceutical.

3) I currently am the Chief Scientific Officer of the assignee for the captioned patent application. As such, I am responsible for, among other things, developing dietary supplement formulations and assessing the clinical support for dietary supplement labeling claims.

4) I am the inventor of record of United States Letters Patent No. 6,420,350, United States Published Patent Application No. 2002/0136781, and several others. I am the inventor of record of one of the references which is cited against the immediate application.

5) I therefore respectfully believe that I am one of skill in the art.

6) I have reviewed the art of record in this case, including Fanie Retief VAN HEERDEN *et al.*, *Pharmaceutical Compositions Having Appetite Suppressant Activity*, U.S. Letters Patent No. 6,376,657 and *Phytopharm boosts P57 Production*, Market letter (10 December 2001).

7) I have also reviewed the OFFICE ACTION dated 18 July 2005. I respectfully disagree with certain of the facts alleged by the OFFICE ACTION.

8) The OFFICE ACTION at page 3 says:

> Van Heerden et al. clearly and beneficially teach a weigh loss composition which comprises Hoodia gordonii as an active ingredient therein, as well as a method of reducing weight in a subject in need thereof via administering an effective amount of the Hoodia gordonii extract.

I respectfully disagree with certain of the facts asserted by this statement. I infer that the factual misstatements are based on an inaccurate factual assumption regarding the relationship between appetite suppression and weight loss.

Appetite Suppression Is Not Weight Loss

9) Appetite suppression is not the same thing as weight loss. To the contrary, one may reduce body weight without suppressing appetite; this may be done, for example, by increasing the animal's rate at which it metabolizes calories (e.g., by increasing physical activity).

10) Similarly, one may suppress appetite and not affect body weight. This is because reducing food intake may slow the body's metabolic rate, allowing the body to maintain its weight despite a lower caloric intake. This is why transient dieting is not considered effective to reduce body weight.

11) VAN HEERDEN confirms this. VAN HEERDEN demonstrates that fenfluramine (the reference standard appetite suppression drug) causes appetite suppression but does not cause weight loss. Example 44 says, "The reference standard, fenfluramine (7.5 mg/kg), produced statistically significant reductions in food consumption at 6 and 24 hours post-dose when compared with the relevant vehicle-treated control group. No statistically significant effects on water consumption or bodyweight were recorded." Column 57, lines 18 to 24 (emphasis added). VAN HEERDEN therefore teaches that fenfluramine-induced appetite suppression has no effect on body weight.

12) Similarly, VAN HEERDEN demonstrates that a newly-discovered chemical, 3-0-[-ß-D-thevetopyranosylcymaropyranosyl]-12ß-0-tigloyloxy-14ß-hydroxy-14-pregn-50-en-20-one, causes appetite suppression without weight loss. Example 44 says, "Sample 3 (active moiety) produced statistically significant reductions in food consumption at an oral dose of 5.0 mg/kg. No statistically significant effects on bodyweights were produced by the active moiety." *Id.* at column 57, lines 10 to 15 (emphasis added). VAN

HEERDEN therefore teaches that Sample 3-induced appetite suppression has no effect on body weight.

13) VAN HEERDEN thus confirms what one of skill in the art would know already – that appetite suppression alone does not affect body weight. Appetite suppression and weigh loss are two different clinical phenomena.

One Of Skill In The Art Would
Read VAN HEERDEN *Et Al.* To
Teach An Appetite Suppressant

14) One of skill in the art would read VAN HEERDEN to teach a compound for appetite suppression. VAN HEERDEN is titled, "Pharmaceutical Compositions Having Appetite Suppressant Activity." The Abstract teaches that VAN HEERDEN teaches "an appetite suppressant agent." The Specification begins, "the invention relates to an appetite suppressant agent, to a process for synthetically producing the appetite suppressant agent, to a process for extracting the appetite suppressant agent from plant material, to an appetite suppressant composition containing the appetite suppressant material, and to a method of suppressing an appetite." *Id.* at column 1, lines 16 to 23.

15) Thus, one of skill in the art would read VAN HEERDEN to teach an appetite suppressant.

One Of Skill In The Art Would Not Read VAN
HEERDEN To Teach A Weight Loss Composition

16) One of skill in the art would read VAN HEERDEN to teach appetite suppression. One of skill in the art would not, however, read VAN HEERDEN to teach a compound for weight loss. To the contrary, VAN HEERDEN teaches an "active moiety" (3-0-[-ß-D-

thevetopyranosylcymaropyranosyl]-12ß-0-tigloyloxy-14ß-hydroxy-14-pregn-50-en-20-one) which induces transient appetite suppression, but also induces a net weight ***gain***.

VAN HEERDEN Teaches That *Hoodia* Extracts
Cause Body Mass To Increase, Not Decrease

17) VAN HEERDEN teaches that hoodia extracts cause body mass to increase, not decrease. VAN HEERDEN provides ample experimental data showing this. The reference summarizes this data in Figures 6 and 5 (copies attached).

Figure 6

18) Figure 6 measures net change in body mass over a one week period following administration of a variety of test compounds. Some of the tested groups lost body mass, and some gained body mass, over the study period.

19) The group which clearly lost the most weight is Group 5. Group 5 lost 10.45% of body mass over the test period. Group 5 is the control group. Group 5 was not administered *hoodia gordonii* extract, nor 3-0-[-ß-D-thevetopyranosylcymaropyranosyl]-12ß-0-tigloyloxy-14ß-hydroxy-14-pregn-50-en-20-one.[1]

20) In contrast, Groups 1, 2, 3, and 4 retained significantly more body mass. Groups 3 and 4 lost less body mass than Group 5. Groups 1 and 2 actually *gained* body mass. Groups 1 to 4 were administered *hoodia gordonii* sap. Groups 1 to 4 therefore show that *hoodia gordonii* causes an animal to retain (or even gain) body mass, not lose it. Groups 1 to 4

[1] This is in line with experimental error, because VAN HEERDEN shows that rats can have a 10% per week weight variation, without having any appetite-affecting substance at all. This is shown by comparing Group 9 in Figure 5 and in Figure 6. Group 9 experienced a 3.51% weight loss over two weeks (shown in Figure 5), yet, as shown in Figure 6, a 9.59% gain in the second week. This shows an 11.95% weight loss during the first week, followed by a 9.59% gain. This is significant because it indicates that body mass can fluctuate 10% per week without having any active substance at all.

thus teach that *hoodia gordonii* extract may be effective to cause weight gain, not weight loss. This teaches away from my own invention.

21) Similarly, Group 6 shows a significant increase in body mass, while Groups 7 and 8 show little change. Groups 6, 7 and 8 were administered dried *hoodia gordonii* sap. Groups 6, 7 and 8 thus teach that *hoodia gordonii* may be effective to cause body mass gain, not loss. This teaches away from my own invention.

Figure 5

22) Figure 5 confirms this. Figure 5 measures net change in body mass over the week after administration of the appetite-suppressing compounds, and the week before administration of the appetite-suppressing compounds. Figure 5 thus provides data on normal weight variation before administering any appetite-suppressing compounds.

23) Notably, all tested groups lost weight over the two week period. (This could be because the test subjects lacked adequate sleep or physical activity during the fourteen day test, or disliked the food they were given, etc...) While all groups lost weight, however, some groups lost less weight than others.

24) The group which lost the most weight is Group 5. Group 5 lost 18.91% of body mass over the test period. Group 5 is the control group. Group 5 was not administered *hoodia gordonii* extract nor 3-0-[-ß-D-thevetopyranosylcymaropyranosyl]-12ß-0-tigloyloxy-14ß-hydroxy-14-pregn-50-en-20-one.

25) In contrast to Group 5, Groups 1, 2, 3, and 4 retained more body mass than Group 5. Group 3 and 4 lost less body mass than Group 5, and Group 1 and 2 actually *gained* body mass. Groups 1 to 4 were administered *hoodia gordonii* sap. Groups 1 to 4 therefore show that *hoodia gordonii* causes an animal to retain body mass, not lose it. Groups 1 to

4 thus teach that *hoodia gordonii* is effective to prevent weigh loss, not cause weight loss. This teaches away from my own invention.

26) Groups 6, 7 and 8 retained more body mass than control Group 5.

Figures 5 and 6 Together

27) VAN HEERDEN teaches the results of a two week study. Body mass was measured at the beginning. The ensuing first week was a control week, without any appetite-affecting substances administered to any group. At the end of the first week, body mass was again measured and test compounds were administered. One week after administration, body mass was again measured. Figure 6 provides the results for the week after administration (days 0 to 7). Figure 5 provides the results for the entire two week period (day -7 to day +7). VAN HEERDEN, however, neglects to graphically provide the results for the first week (day -7 to 0). We can, however, derive the results for this first week, by subtracting the results from the second week (Figure 6) from the results for the two weeks together (Figure 5).

28) The results for the first week teach that hoodia administration causes body mass increase, even in animals normally expected to lose body mass.

29) Group 6, for example, shows a 5% increase in body mass in the second week (the week following administration).[2] *See* Figure 6. For the entire two week period, Group 6 shows a 6% decrease in body mass. *See* Figure 5. This means that Group 6 lost 10% of its body mass during the week before administration of hoodia sap. (Losing about 10% the first week, and gaining back about 5% the second week, leaves a net change of about 6% for the two weeks taken together) This is in line with Group 5, the control group which also

[2] I round these percentages to the nearest whole number.

lost about 10% in body mass per week. In the week following administration, however, Group 6 gained body mass, rather than losing it. Group 6 therefore teaches that dried *hoodia gordonii* causes body mass to increase, even in subjects who would ordinarily be expected to lose body mass.

30) Group 7 confirms this. Group 7 shows a 1% increase in body mass in the second week (the week following administration). *See* Figure 6. For the entire two week period, Group 7 shows a 10% decrease in body mass. *See* Figure 5. This means that Group 7 lost 11% of its body mass in the week before administration of hoodia sap. This means that Group 7 lost 11% of its body mass before administration of hoodia sap, and gained 1% following administration. Group 7 therefore teaches that dried *hoodia gordonii* causes body mass to increase, even in subjects who would ordinarily be expected to lose body mass.

31) Group 8 confirms this. Group 8 shows a 1% decrease in body mass in the second week. *See* Figure 6. For the entire two week period, Group 8 shows a 14% decrease in body mass. *See* Figure 5. This means that Group 8 lost 15% of its body mass in the week before administration of hoodia sap. This means that Group 8 lost 15% of its body mass before administration of hoodia sap, and gained 1% following administration. Group 8 therefore teaches that dried *hoodia gordonii* causes body mass to increase, even in subjects who would ordinarily be expected to lose body mass.

32) Group 1 shows a 1% increase in body mass in the second week. *See* Figure 6. For the entire two week period, Group 1 shows a 9% decrease in body mass. *See* Figure 5. This means that Group 1 lost 11% of its body mass in the week before administration of

hoodia and gained 12% following administration. Group 1 therefore teaches that *hoodia gordonii* sap causes body mass to increase, even in subjects who would ordinarily be expected to lose body mass.

33) Group 2 shows a 4% increase in body mass in the second week. *See* Figure 6. For the entire two week period, Group 2 shows a 7% decrease in body mass. *See* Figure 5. This means that Group 2 lost 11% of its body mass in the week before administration of hoodia and gained 15% following administration. Group 2 therefore teaches that *hoodia gordonii* sap causes body mass to increase, even in subjects who would ordinarily be expected to lose body mass.

34) Group 3 shows a 2% decrease in body mass in the second week. *See* Figure 6. For the entire two week period, Group 3 shows a 12% decrease in body mass. *See* Figure 5. This means that Group 1 lost 10% of its body mass in the week before administration of hoodia and lost only 2% following administration. Group 3 therefore teaches that *hoodia gordonii* sap slows body mass loss – that is, it causes body mass to be conserved in subjects who would ordinarily be expected to lose body mass more rapidly.

35) Group 4 shows a 5% decrease in body mass in the second week. *See* Figure 6. For the entire two week period, Group 4 shows a 17% decrease in body mass. *See* Figure 5. This means that Group 4 lost 12% of its body mass in the week before administration of hoodia and lost only 5% following administration. Group 4 therefore teaches that *hoodia gordonii* sap slows body mass loss – that is, it causes body mass to be conserved in subjects who would ordinarily be expected to lose body mass more rapidly.

36) Thus, Groups 1, 2, 6, 7 and 8 teach that dried *hoodia gordonii* causes body mass to increase, even in subjects who would ordinarily be expected to lose body mass. Groups 3 and 4 teach that *hoodia gordonii* sap slows body mass loss in subjects who would ordinarily be expected to lose body mass more rapidly. All of these teach away from my own invention.

Figure 2

37) VAN HEERDEN teaches a possible reason for his test compounds to increase body mass. VAN HEERDEN summarizes this at Figure 2 (copy attached).

38) Figure 2 shows daily food intake following administration of a methanol extract of *trichocaulon piliferum*. Figure 2 shows rats' basal rate of food intake (shown at days 3-5) remains roughly constant at 17 grams of food per day.

39) After administering sap from *trichocaulon piliferum* (at day 5), however, the rats' rate of food intake transiently decreases quite sharply.

40) This period of reduced food intake, however, is transient. It is immediately followed by a prolonged period of *increased* food intake.

41) I suspect that VAN HEERDEN's *trichocaulon piliferum* compound transiently suppresses appetite, which in turn lowers the animal's metabolic rate, leaving the animal less able to quickly metabolize the subsequent increased caloric intake.

VAN HEERDEN Teaches 3-0-[-ß-D-thevetopyranosylcymaropyranosyl]-12ß-0-tigloyloxy-14ß-hydroxy-14-pregn-50-en-20-one, Not *Hoodia*

42) VAN HEERDEN does not teach nor claim a new use of the *hoodia* plant; to the contrary, VAN HEERDEN teaches the use of 3-0-[-ß-D-thevetopyranosylcymaropyranosyl]-12ß-0-tigloyloxy-14ß-hydroxy-14-pregn-50-en-20-one. See claims.

43) I advocate the opposite. I believe that the *hoodia* plant itself, rather than a chemical extract of it, can be used to safely and effectively control obesity. My solution lies not in a specific chemical present in the *hoodia* plant, but in the timing of the *hoodia* administration.

44) VAN HEERDEN replicated in laboratory rats the incidental (one-time) administration of *hoodia*. He shows that a one-time administration creates a transient appetite suppression phase (in his Figure 2, with the amount used, perhaps 48 hours), followed by an appetite stimulation phase of indeterminate duration. I propose repeat administration, before the onset of the appetite stimulation phase. In other words, the administration occurs at least as frequently as the length of the appetite suppression phase.

45) For example, my pending claims require repeat *hoodia* administration at least once every about 48 hours or, in any case, before the appetite-stimulating effect occurs.

46) In contrast to VAN HEERDEN, I also advocate longer-term administration, repeated over a period of weeks or months. When this repeat-administration is practiced over an extended period of time (at least 30-45 days), this may enable the user's body to adjust to a lower basal body weight, and thereby eventually perhaps eliminate the appetite stimulation phase altogether, and thus avoiding the eating binge -and weight gain- that follows incidental *hoodia* administration.

Contrary To The Teachings Of VAN HEERDEN, I Have
Shown That *Hoodia Gordonii* Is Effective For Weight Loss

47) Contrary to the teachings of VAN HEERDEN, I have shown that *Hoodia gordonii* is effective for weight loss. I have tested Hoodia gordonii administered to human subjects in several different dosage amounts. My results show that my claimed invention appears

to cause statistically-significant decreases in body mass in human test subjects. I here append the clinical results for two different studies on two different daily dosages of *Hoodia gordonii*.

48) The first study evaluated the clinical effect of placebo and Hoodia on body mass. For this study, I asked the scientific consulting organization of Marshall–Blum (Bangor, Maine) to test the efficacy of my invention.

49) The testing was performed according to the *Marshall – Blum Standard Operating Procedure* (SOP) (21 April 2004) for dietary supplement testing. These procedures govern how human test subjects are selected, how records are maintained, and other factors to assure the reliability of the experimental data produced. I attach a copy of this document as an exhibit.

50) This testing was also performed according to the *Marshall – Blum Product formulation Due Diligence* (3 May 2004). These procedures govern how compounds are selected for testing and other factors to assure the reliability of the experimental data produced. I attach a copy of this document as an exhibit.

51) They provided their experimental data in a report titled, *Dietary Supplements to Promote Healthy Weight Management*.

52) This raw experimental data was statistically analyzed by Thomas E. Wasser, Ph.D. I enclose a copy of his 5 June 2005 report. This report refers to my invention variously as the "supplement," or by the specific formulation name (X-32; Super X-32).

53) Dr. Wasser reports, "exercise alone (Placebo) leads to weight loss, there is also evidence that exercise with supplement leads to more significant weight loss than exercise alone."

See id. at page 5, Section 2. Dr. Wasser concludes, "In my opinion there is considerable evidence to conclude that both the X32 and Super X-32 products are having relevant effects on weight loss as compared to Placebo alone." *Id.* at pages 5-6.

54) This finding was confirmed in a second, independent study. That study was performed by International Research Services, Inc. (Port Chester, New York) according to *A Double-Blind, Randomized, Parallel Design, Placebo-Controlled Clinical Evaluation ...*, Protocol No. 3023GTC0904 (8 October 2004) (copy enclosed). The resulting experimental data was analyzed by Consult.Stat Statistical Services (Macungie, Pennsylvania). That analysis concludes, "subjects lost significantly more weight on the Trim Spa Product than did the Control group." *See* Thomas E. Wasser, Letter (17 April 2005) (copy enclosed) at page 4 (emphasis in original).[3]

55) The "CONCLUSIONS DRAWN FROM THE STUDY" address safety but also, more relevantly, I have found that 74% of the human test subjects taking Hoodia at the claimed amounts achieved a measurable reduction in body mass after twelve weeks of use.

56) The "SUMMARY OF WEIGHT LOSS RESULTS" concludes "with confidence" that the claimed invention is "significantly superior" to placebo in generating weight loss.

57) Our results would not have been expected by one of skill in the art at the time I made my invention.

58) There is a nexus between this evidence and the pending patent claims, because this evidence would be considered by one of skill in the art to have probative value in

[3] The final report refers to the tested product by the name of the manufacturer (the "Trim Spa Product") rather than the precise name of the test composition.

showing the pending patent claims are enabled and are non-obvious in light of the contrary teachings of the art of record.

59) I therefore respectfully believe that my pending claims are not obvious in light of VAN HEERDEN.

The San Tribesmen Used Hoodia For Water,
Rather Than For Appetite Suppression

60) As a final matter, I would like to correct a statement made in the Specification, regarding the prior art. As filed with the Patent Office, the patent Specification at page 3, lines 5 *et seq.*, says:

> *Hoodia gordonii* is a cactus. It has been used for years by the San tribesmen in South Africa to temporarily prevent hunger during extended hunting expeditions, during which food might not have been readily available. This use occurred as early as 1937, when a Dutch anthropologist studying the San noted their use of the *Hoodia* cactus.

Since the date that this patent application was filed, I have learned that this statement is not correct. To the contrary, Dr. Marthinus HORAK, a scientist at South Africa's Council for Scientific and Industrial Research, says that "the oft-quoted story that the San ate Hoodia to stave off hunger is 'nonsense'." *See* Laura JOHANNES, *Hoodia's Hunger Claims*, Wall Street Journal page D5 (13 December 2005) (copy attached). Rather, Dr. HORAK says that the San "do occasionally consume [*hoodia*] for its water content." *Id.* Thus, it appears that the San did in fact consume hoodia, albeit for its water content, not for appetite suppression. I apologize for any confusion this may have caused.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon or any patent to which this verified statement is directed.

Albert M. Fleischner

Albert M. FLEISCHNER, Ph.D.

Dated as of Wednesday, December 21, 2005

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